510(k) SUMMARY

DEC 2 0 2005

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K052889.

Submitter Information

Address:	Fujirebio Diagnostics, Inc. 201 Great Valley Parkway Malvern, PA 19355
Contact person:	Diana L. Wolaniuk, (610) 240-3917
Summary preparation date:	December 12, 2005

Name of Device

Trade/Proprietary Name:	VITROS Immunodiagnostics Products CA 19-9 Reagent Pack VITROS Immunodiagnostics Products CA 19-9 Calibrators VITROS Immunodiagnostics Products CA 19-9 Range Verifiers
Common/Usual Name:	CA 19-9 Assay
Classification Name:	System, Test, Carbohydrate Antigen (CA19-9), For Monitoring And Management Of Pancreatic Cancer

Predicate Device

Fujirebio Diagnostics, Inc. CA 19-9 RIA

Device Description

The VITROS CA 19-9 assay is performed using the VITROS CA 19-9 Reagent Kit and the CA 19-9 Calibrator Kit on the VITROS Immunodiagnostic System. An immunometric techniques is used, 1116-NS-19-9 defined antigen present in the sample reacts with a biotinylated antibody (mouse monoclonal anti-1116-NS-19-9 defined antigen). The antigen-antibody complex is captured by streptavidin on the wells, unbound materials are removed by washing. In a second incubation a horseradish peroxidase (HRP)-labeled antibody conjugate (mouse monoclonal anti-1116-NS-19-9 defined antigen) binds to the immobilized 1116-NS-19-9 defined antigen. Unbound conjugate is removed by washing. The bound HRP conjugate is measured by a luminescent reaction. A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent, is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs the emission. The light signals are read by the VITROS System. The amount of HRP conjugate bound is directly proportional to the concentration of 1116-NS-19-9 defined antigen present.

The system is comprised of three main elements:

1. The VITROS Immunodiagnostic Products (in this case VITROS Immunodiagnostic Products CA 19-9 Reagent Pack, VITROS Immunodiagnostic Products CA 19-9 Calibrator Kit, and the VITROS Immunodiagnostic Products CA 19-9 Range Verifier Kit, which are combined by the VITROS Immunodiagnostic System to perform the VITROS CA 19-9 assay).
2. The VITROS Immunodiagnostic System – instrumentation, which provides automated use of the immunoassay kits. The VITROS Immunodiagnostic System was cleared for market by a separate 510(k) premarket notification (K962919).
3. Common reagents used by the VITROS System in each assay. The VITROS Immunodiagnostic Products Signal Reagent and VITROS Immunodiagnostic Products Wash Reagent were cleared as part of the VITROS Immunodiagnostic Products Total T3 510(k) premarket notification (K964310).

The VITROS System and common reagents are dedicated specifically only for use with the VITROS Immunodiagnostic Products range of immunoassay products.

Intended Use

Reagent Kit
For the *in vitro* quantitative measurement of 1116-NS-19-9 defined antigen in human serum and plasma (EDTA or heparin). The VITROS CA19-9 assay is to be used to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The VITROS CA19-9 assay can be used to monitor the disease status in patients with confirmed pancreatic cancer who show measurable CA19-9 values over the course of their disease. Serial CA19-9 test results should be used in conjunction with all other available clinical and laboratory data before a medical decision is determined.

Calibrator Kit
For *in vitro* use in the calibration of the VITROS Immunodiagnostic System for the quantitative measurement of 1116-NS-19-9 defined antigen in human serum and plasma (EDTA or heparin).

Range Verifier Kit
For *in vitro* use in verifying the calibration range of the VITROS Immunodiagnostic System when used for the measurement of 1116-NS-19-9 defined antigen.

WARNING: Patients known to be genotypically negative for the Lewis blood group antigen will be unable to produce the CA 19-9 antigen even in the presence of malignant tissue. Phenotyping for the presence of the Lewis antigen may be insufficient to detect true Lewis antigen negative individuals. Even patients who are genotypically positive for the Lewis antigen may produce varying levels of CA 19-9 based on gene dosage effect.

Statement of Substantial Equivalence

For the *in vitro* quantitative measurement of 1116-NS-19-9 defined antigen in human serum and plasma (EDTA or heparin). The VITROS CA19-9 assay is to be used to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The VITROS CA19-9 assay can be used to monitor the disease status in patients with confirmed pancreatic cancer who show measurable CA19-9 values over the course of their disease. Serial CA19-9 test results should be used in conjunction with all other available clinical and laboratory data before a medical decision is determined.

VITROS CA 19-9 Assay kit is substantially equivalent to Fujirebio Diagnostics, Inc. CA 19-9 RIA. Both of the devices are IVD products and are indicated for the quantitative determination of CA 19-9 assay values (1116-NS-19-9 reactive determinants) and as aids in monitoring disease status for patients with pancreatic cancer.

A comparison of the features of the VITROS CA 19-9 Assay device and the Fujirebio Diagnostics, Inc. CA 19-9 RIA follows.

	Ortho Clinical Diagnostics VITROS Immunodiagnostic Products CA 19-9™ Assay (Proposed Device)	**Fujirebio Diagnostics, Inc. CA 19-9™ RIA (Predicate Device) K020566**
Device Type	*In vitro* diagnostic	*In vitro* diagnostic
Classification and Product Code	Class II, NIG	Class II, NIG
Principle of Operation	Enzymatic Immunoassay (EIA)	Radioimmunoassay (RIA)
Product Usage	Clinical and Hospitals laboratories	Clinical and Hospitals laboratories
Intended Use	For the *in vitro* quantitative measurement of 1116-NS-19-9 defined antigen in human serum and plasma (EDTA or heparin). The VITROS CA19-9 assay is to be used to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The VITROS CA19-9 assay can be used to monitor the disease status in patients with confirmed pancreatic cancer who show measurable CA19-9 values over the course of their disease. Serial CA19-9 test results should be used in conjunction with all other available clinical and laboratory data before a medical decision is determined.	The Fujirebio Diagnostics CA 19-9™ RIA, an *in vitro* diagnostic test for the quantitative measurement of the CA 19-9 tumor associated antigen, in human serum or plasma, is indicated for the serial measurement of CA 19-9 to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The test is useful to aid in: *Monitoring of disease status in those patients having confirmed pancreatic cancer who have levels of serum or plasma CA 19-9 above the cutoff, at the time of diagnosis.* CA 19-9 values must be interpreted in conjunction with all other clinical and laboratory data before a medical decision is determined.
Type of Specimen	Human serum or plasma (EDTA, Sodium and Lithium Heparin)	Human Serum or Plasma (Citrate, Heparin, ACD-A or EDTA)
Specimen Collection Method	Routine Phlebotomy Techniques	Routine Phlebotomy Techniques
Capture Antibody	1116-NS-19-9 (F(ab')2) mouse monoclonal	1116-NS-19-9 mouse monoclonal
Conjugate Antibody	1116-NS-19-9 (F(ab')2) mouse monoclonal	1116-NS-19-9 mouse monoclonal
Standards/Calibrators	3 levels (1 = 15 U/mL, 2 = 60, 3 = 700 U/mL)	6 levels (0 - 240 U/mL)
Interpretation of Results	Calibrator Curve	Standard Curve

Comparison Study

A total of 176 specimens were evaluated for the correlation analysis using the VITROS CA 19-9 assay and the Fujirebio Diagnostics, Inc. CA 19-9 RIA. The VITROS CA 19-9 assay specimen range was 1.7 – 653 U/mL and for the Fujirebio Diagnostics CA 19-9 RIA assay specimen range was 2.36 – 892 U/mL.

The Passing-Bablok regression analysis comparing the VITROS CA 19-9 assay to the Fujirebio Diagnostics, Inc. CA 19-9 RIA resulted in a slope of 0.83 (95% confidence interval of 0.80, 0.88) and an intercept of –4.02 (95% confidence interval of –1.3, 0.27). The Spearman correlation coefficient was 0.93 (95% confidence interval of 0.91, 0.95).

Pancreatic Cancer Serial Specimens

This analysis is based on 74 patients. There were a total of 261 evaluable observations. The average number of observations per patient is 3.5.

The average age of the subjects at time of diagnosis was 61.8 years (Exact 95% CI: 59.5 years to 64.1 years) with a range of 41 to 85 years. Fifty-five percent (55% or 41/74) of the 74 patients were men and the remaining forty-five percent (45% or 33/74) were women. Staging was available from the chart for 70 of the 74 patients. The majority of the patients were stage III and IV (41.9% for both stages) while 4.1% and 6.8% were stage I and II respectively.

Association between Change in Marker Value and Change in Disease State

A 2x2 table was constructed to show the association between a positive change in a patient's CA 19-9 value and progression of the disease from one observation to the next. A significant positive change in VITROS CA 19-9 level was defined as at least a 12.5% increase in assay value [at least 2.5 times greater than the %CV of the test]. The following table (entitled "Distribution of W by V") presents the results for the 187 observation pairs in this study.

Three estimates of Concordance are given for the following Table.

Total Concordance: $C = (15+96) / 187 = 111/187 = 59.4\%$

Positive Concordance: $C_+ = 15/33 = 45.5\%$

Negative Concordance: $C_- = 96/154 = 62.3\%$

Distribution of W by V

Change in CA 19-9 (V)	Change in Disease State (W)		Total
	Progression	No Progression	
≥ 12.5%	15	58	73
< 12.5%	18	96	114
Total	33	154	187

Per Patient Analysis

The table below (entitled " Per Patient Distribution) demonstrates this distribution for the 74 patients in this study.

Per-Patient Distribution

Change in CA 19-9	Change in Disease State		Total
	Progression	No Progression	
≥ 12.5%	15	18	33
< 12.5%	7	34	41
Total	22	52	74

Estimates of per-patient concordances can be obtained. Confidence intervals for these estimates can be determined using the binomial distribution. The following table (entitled" Estimate of Per-Patient Positive, Negative and Total Concordance with 95% confidence Intervals) demonstrates the estimates and 95% confidence intervals about each estimate.

Estimates of Per-Patient Positive, Negative and Total Concordance with 95% Confidence Intervals

Statistic	Estimate	Lower Bound	Upper Bound
C	66.22%	54.28%	76.81%
C_+	68.18%	45.13%	86.14%
C_-	65.38%	50.91%	78.03%

In addition to the studies mentioned above, tests were performed to obtain analytical sensitivity, specificity, precision, dilution linearity, and expected values. Refer to the VITROS CA 19-9 assay Instructions For Use for VITROS CA 19-9 assay results

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Fujirebio Diagnostics, Inc.
c/o Ms. Diana L. Wolaniuk
Clinical and Regulatroy Affairs Specialist
201 Great Valley Pkwy,
Malvern, PA 19355-1307

DEC 2 0 2005

Re: k052889
Trade/Device Name: VITROS Immunodiagnostics Products CA 19-9™ Reagent Pack
VITROS Immunodiagnostics Products CA 19-9™ Calibrators
VITROS Immunodiagnostics Products CA 19-9™ Range Verifiers
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-associated Antigen Immunological Test System
Regulatory Class: Class II
Product Code: NIG, JIT, JJX
Dated: October 11, 2005
Received: October 13, 2005

Dear Ms. Wolaniuk:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to legally

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Robert L. Becker, Jr., MD, Ph.D
Director
Division of Immunology and Hematology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K052889

Device Name: VITROS CA 19-9™

Indications For Use:

Reagent Kit
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Range Verifier Kit
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Prescription Use ✓ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K052889